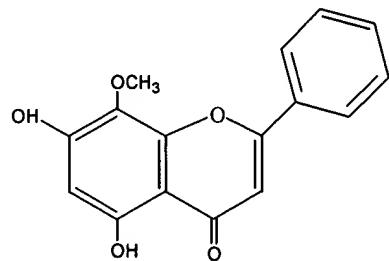


REMARKSRejection of Claims 13-16 and 19-22 Under 35 U.S.C 103(a)

Claims 13-16 and 19-22 have been rejected under 35 U.S.C 103(a), as it is said that they are unpatentable over Cassels *et al.* (US 5,756,538).

The subject application has claims drawn to a method of treating anxiety in a patient in need thereof comprising administering an effective non-toxic dose to the patient of a compound referred to as wogonin, having the formula:



Cassels *et al.* describe flavonoids, flavonone derivatives and biflavonoids. The Cassels *et al.* patent describes in particular seven preferred subgeneruses of compounds having general formula (I) (column 3, lines 16-29) and a number of preferred compounds (column 3, lines 31-34). One of the seven subgeneruses set forth as being preferred is a subgenus "wherein R<sup>3</sup> and R<sup>1</sup> are both hydroxy." R<sup>3</sup> and R<sup>1</sup> are positions 7 and 5, respectively, of flavone. A general statement is made in the patent (column 2, lines 1-9) that the described compounds have anxiolytic properties. However, only diazepam, chrysin, 2'-fluorochrysin, 2'-bromochrysin, 6, 8-dibromochrysin, apigenin, and 7-bromoflavone were tested for anxiolytic effects in rats.

The Examiner has stated in the Office Action of 22 August 2003:

However, it would have been *prima facie* obvious to a person of ordinary skill in the art, at the time the claimed invention was made, to treat anxiety by employing a flavone with hydroxyl groups at 5 and 7, and a methoxyl group at position 8 (R<sup>4</sup> as depicted by Cassels)." A person of ordinary skill in the art would have been motivated to treat anxiety by employing a flavone with hydroxyl groups at 5 and 7, and a methoxyl group at position 8 (R<sup>4</sup>

as depicted by Cassels) because Cassels expressly prefer flavone with 5 and 7 dihydroxyl groups and methoxyl group is known to be useful as a substituent at position 8 (R4). The selection of methoxyl group herein is seen to be a selection from amongst equally suitable functional groups and as such obvious. Ex parte Winters 11 USPQ 2<sup>nd</sup> 1387 (at 1388).

This is not the correct analysis. *The Manual of Patent Examining Procedure* (MPEP) devotes section 2144.08 to “Obviousness of Species When Prior Art Teaches Genus.” Patent examiners are to follow a flowchart (page 2100-150 of MPEP -- February 2003 revision of 8<sup>th</sup> edition) to determine whether a *prima facie* case of obviousness can be found. The flowchart states at the top, “If the closest prior art is a single reference disclosing a genus, determine whether the claimed species or subgenus would have been obvious to one of ordinary skill in the pertinent art at the time the invention was made by performing the following analysis.” In the present case, the cited prior art is a single reference disclosing a genus; a species within this genus is claimed.

The patent examiner is to first consider the “Graham factors.” A claimed invention is unpatentable if the differences between it and the prior art “are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art.” See *Graham v. John Deere Co.*, 383 U.S. 1, 14, 86 S.Ct 684, 15 L.Ed.2d 545, 148 USPQ 459, 465 (1966), which set forth factors to be considered: (1) the scope and content of the prior art; (2) the level of ordinary skill in the prior art; (3) the differences between the claimed invention and the prior art; and (4) objective evidence of nonobviousness. The Examiner has not expressed reliance on any of these “Graham factors” to make a *prima facie* case of obviousness.

To establish a *prima facie* case of obviousness, the patent examiner is next to determine whether there would have been motivation to select the claimed species.

If Cassels *et al.* teach a method of treating anxiety in a patient by administering to the patient a compound that would fall into the described (column 3, lines 16-19) “compounds of general formula (I) wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup> and R<sup>5</sup> may independently be H, OH or halo (including F, Cl, Br or I) are preferred,” then a large number of methods are taught, corresponding to the large number of compounds that would fall into this genus of compounds. The Examiner has not pointed out any express teachings in the prior art that would have motivated the selection of the

subgenus method of treating anxiety by administering "flavone with 5 and 7 dihydroxyl groups" from among the seven subgenera indicated as preferred, and further, has not pointed out any express teachings that would have motivated the selection of a method of treating anxiety by administering wogonin from the many methods to be selected from based on the many permutations of the compound of general formula (I).

Further, it is incorrect to assume that "[t]he selection of methoxyl group herein is seen to be a selection from amongst equally suitable functional groups . . ." It is the obviousness or nonobviousness of the invention *as a whole* that must be considered. Here, the invention is a method of treating anxiety in a patient; the invention is not a compound or subgenus of compounds. Cassels *et al.* do not report data that would lead to the conclusion that compounds within the subgenus flavone with hydroxyl groups at positions 5 and 7 are superior as anxiolytic agents. Cassels *et al.* do not report any data on the biological activity of wogonin that would indicate its efficacy as an anxiolytic agent. Table II in column 10 of Cassels *et al.* shows the results of an experiment in which various flavonoids were tested for their ability to compete with  $^3\text{H}$ -flunitrazepam for the benzodiazepine receptor. The  $\text{IC}_{50}$  values, indicating affinity for the benzodiazepine receptor, from which anxiolytic activity may be inferred, vary by 8,000 fold for the fifteen compounds tested, demonstrating the unpredictable effects of substituting one functional group for another. Thus, the suitability of wogonin as an anxiolytic agent could not have been predicted.

The Examiner has not pointed out any teachings from the prior art that would have motivated one of ordinary skill in the art to select the claimed species. Therefore, a *prima facie* case of obviousness has not been established.

**CONCLUSION**

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned.

Respectfully submitted,

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